Epitomes

Important Advances in Clinical Medicine

Internal Medicine

The Scientific Board of the California Medical Association presents the following inventory of items of progress in internal medicine. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome, and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, research workers or scholars to stay abreast of these items of progress in internal medicine that have recently achieved a substantial degree of authoritative acceptance, whether in their own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on Internal Medicine of the California Medical Association and the summaries were prepared under its direction.

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Use of Ipratropium Bromide in Chronic Obstructive Pulmonary Disease

INHALED ANTIMUSCARINIC AGENTS (atropine sulfate, atropine methylnitrate, ipratropium bromide) can partially relieve airflow obstruction in patients with chronic obstructive pulmonary disease (COPD) by reducing vagally mediated bronchomotor tone. Ipratropium bromide (Atrovent) in metered-dose inhaler form has recently been approved by the Food and Drug Administration for use as a bronchodilator in COPD. Bronchodilation following the use of ipratropium occurs within minutes (slower than with adrenergics) and lasts four hours or more (comparable with adrenergics). Maximal bronchodilation is achieved with metered doses of 40 to 80 μg; the recommended therapeutic dose is two actuations (20 μg per actuation) of the metered-dose inhaler. The major therapeutic advantage of ipratropium (a quaternary ammonium derivative) over atropine (a tertiary ammonium compound) is its poor absorption after inhalation, so that few atropinic side effects occur even with large doses. In therapeutic doses, it has no significant effect on mucus production, viscosity or clearance and, unlike β_2-selective agonists, it does not cause tremor.

A recent double-blind multicenter trial of ongoing therapy with metered doses of ipratropium (40 μg) versus metaproterenol sulfate (1,500 μg) four times a day for 90 days in patients with COPD showed a significantly greater magnitude and duration of bronchodilation in the ipratropium-treated group, which was sustained throughout the three months of the study. Side effects from both agents were infrequent, but tachyphylaxis, obvious with the β-agonist, was less evident with ipratropium. These findings, together with similar results from several smaller-scale studies, support consideration of ipratropium as a first-line bronchodilator in the maintenance treatment of COPD.

Although a large dose of either an antimuscarinic or a β-agonist compound administered alone produces maximal bronchodilation in patients with COPD, at least one study has shown additive bronchodilation in these patients when conventional therapeutic doses of ipratropium and a β-agonist were combined. Further studies are required to evaluate the advantages of combining ipratropium with a β-agonist or theophylline (or both) in the long-term management of COPD.

In patients with atopic asthma, unlike in those with COPD, antimuscarinic agents often cause less bronchodilation than do β-agonists; consequently, ipratropium should be considered a second-line bronchodilator in treating allergic asthma.

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The Questionable Value of Routine Admission Urinalyses

TWO RECENT STUDIES questioned the value of the time-honored routine admission urinalysis. Both studies were conducted on internal medicine wards, and both concluded that the impact on patient care of routinely analyzing urine specimens on admission was very small. The findings support the recommendation of the American College of Physicians that no diagnostic tests should be required as routine procedures for patients admitted to hospital.

The major reasons for the test's small impact on patient care are the relatively low diagnostic yield and the even lower likelihood that detected abnormalities represent true disease. By definition, routine admission urinalyses are done for patients without signs or symptoms of urinary tract disorders. Because the prevalence of disease in this group is low, the predictive value of a positive test—the probability that an abnormality represents true disease—also will be low. In addition, many patients admitted to hospital have diseases unrelated to the urinary tract in which transient, self-limited urinary abnormalities are common. Unfortunately, physicians usually cannot tell which findings represent false-posi-

tive results or self-limited abnormalities without additional, otherwise unnecessary, diagnostic testing.

Hundreds of millions of urine specimens are analyzed in the United States each year, costing consumers billions of dollars. It appears that doing these tests based on clinical findings and not simply on hospital admission could decrease medical care costs with little adverse effect on patient care.

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Diagnosing Pulmonary Embolism

THE ORIGINAL UROKINASE STUDY showed that the clinical diagnosis of pulmonary embolism was not specific enough to justify the risks of anticoagulant therapy: only 162 of 906 patients suspected of having pulmonary embolism had it confirmed angiographically. Subsequently, with quantum improvements in the technology of the perfusion lung scan and the development of a clinically useful ventilation scan, there was widespread use of the combined ventilation-perfusion lung scan for clinical decision making. Unfortunately, no prospective, randomized clinical trial had ever been done to validate the concepts of matched and mismatched scan patterns. This overreliance on the ventilation-perfusion lung scan was the subject in 1977 of a controversial editorial in the *Annals of Internal Medicine*. Much of the literature that appeared after the editorial continued to report results on series flawed by selection bias and other problems. Only one large prospective series studying the sensitivity and specificity of lung scan patterns has been reported, and another is in progress. Before commenting any further, I will review some background information on the risks of anticoagulant therapy.

Heparin use is associated with a 5% to 20% rate of hemorrhagic complications and about a 0.5% to 1% fatality rate. Oral anticoagulation with warfarin sodium is associated with complication rates essentially identical to those mentioned for heparin. Because present recommendations are that patients with venous thrombosis, pulmonary embolism or both are treated with both regimens sequentially, the morbidity and mortality are cumulative. In contrast, pulmonary angiography has a 4% major morbidity rate and a 0.25% fatality rate. Also, the careful use of selective, magnified views allows angiography to be used more safely in patients previously thought to be at high risk, and the refinement of nonionic contrast media may further reduce the risk for renal toxicity.

One large prospective study of the relative sensitivity and specificity of various ventilation-perfusion lung scan patterns found that 86% of "high-probability" scans were associated with an abnormal angiogram, whereas 25% to 40% of "low-probability" scans were associated with abnormal angiograms. Perhaps one of the most important results of this study was the finding of such a "high" prevalence of pulmonary embolism in patients with low-probability scans. The study has been criticized for: a possible low case acquisition rate, routinely doing impedance plethysmography of the lower extremities before referring for scanning and angiography, failure to do angiography in all patients who were scanned, using a new, nonstandard ventilation-perfusion scan classification scheme and an overall high prevalence (55%) of venous thromboembolism in all scan categories. Regardless of these criticisms, this is the only modern, prospective comparison of lung scans and angiography available. The Prospective Investigation of Pulmonary Embolism Diagnosis, sponsored by the National Institutes of Health, is not yet completed.

When the uncertainties associated with the various scan patterns are considered and the risks of treatment with anticoagulant drugs are compared with those of angiography, many physicians believe there is a compelling argument to expand the indications for angiography. Based on available information, clinicians should not rely entirely on the ventilation-perfusion lung scan for decision making in patients felt to have pulmonary embolism, but should strongly consider further diagnostic testing, such as pulmonary angiography or tests to document deep vein thrombosis, as the treatment is essentially the same. Obviously, no single set of recommendations can possibly address the myriad permutations of patient presentations, but the available data indicate that relying on lung scans alone will lead to overtreatment of some patients with false-positive high-probability scans and undertreatment of some with false-negative low-probability scans.

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'Routine' Preoperative Laboratory Testing

PATIENTS ADMITTED TO HOSPITAL for an elective operation commonly undergo a battery of "routine" preoperative laboratory testing. This often includes a complete blood and platelet count, prothrombin time, partial thromboplastin time, electrolytes, blood urea nitrogen, creatinine and glucose levels, urinalysis, chest x-ray film and an electrocardiogram. The goal of such examinations is to detect asymptomatic diseases not apparent on a history and physical examination, which if found and treated appropriately before a surgical procedure would minimize the morbidity and mortality accompanying the operation. Recent studies of such clinical practices have found little scientific support or justification for this goal.

The problem lies in the ability of such tests to detect disease processes in otherwise healthy persons in whom the prevalence of such illnesses is low. Examining just the blood tests that are routinely done (12 in number and assuming "normal" to be the mean value of each test in presumably nondiseased persons plus or minus two standard deviations), in only 54% of all healthy persons screened will all 12 test results be in the "normal" range. Thus, the generation of